



National Children's Study International Biobank & Cohort Meeting

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Rationale for the National Children's Study

From The President's Task Force on Environmental Health and Safety Risks to Children, 2000*

- Compared to adults, children are especially vulnerable to environmental exposures – metabolism, behavior
- Exposures to some agents demonstrate potential for serious developmental effects – lead, prenatal alcohol
- Current known exposures of high frequency – pesticides, violence, media
- Numerous high burden conditions with suspected environmental contribution – learning disabilities, autism, diabetes, asthma, birth defects, premature birth
- Existing research too limited in size and scope to answer the questions
- Life-course (longitudinal) design needed to correctly link with multiple exposures and multiple outcomes

* Reappointed 2001 and 2003





PL 106-310: Children's Health Act of 2000



- (a) PURPOSE - ... to authorize NICHD to conduct a national longitudinal study of environmental influences (including physical, chemical, biological, and psychosocial) on children's health and development.
- (b) IN GENERAL - The Director of NICHD shall establish a consortium of representatives from appropriate Federal agencies (including the CDC and EPA) to:
 - (1) plan, develop, and implement a prospective cohort study, from birth to adulthood, to evaluate the effects of both chronic and intermittent exposures on child health and human development; and
 - (2) investigate basic mechanisms of developmental disorders and environmental factors, both risk and protective, that influence health and developmental processes...
- (e) AUTHORIZATION OF APPROPRIATIONS - There are authorized to be appropriated to carry out this section \$18,000,000 for fiscal year 2001, and such sums as may be necessary for each the fiscal years 2002 through 2005.



Study Concepts

- Longitudinal study of children, their families and their environment
- National in scope
- Hypothesis driven
- Environment defined broadly (chemical, physical, behavioral, social, cultural)
- Study common range of “environmental” exposures and less common outcomes (n ~ 100,000)



Study Concepts (cont.)

- Exposure period begins in pregnancy
- Environment & genetic expression
- State-of-the-art technology
 - Tracking
 - Measurement
 - Data management
- Consortium of multiple agencies
- Extensive public-private partnerships
- National resource for future studies



Hypotheses necessary for framing the study



- No single hypothesis
- Assure answers to “big issue” questions
- Hypothesis required for costly elements
- Important for child health & development (prevalence, severity, morbidity, mortality, disability, cost, public health significance)
- Reasonable scientific rationale
- Require the large sample size (~100,000)
- Measurable with study of this size
- Requires longitudinal follow-up



Example Hypotheses

- low-level exposure to nonpersistent pesticides *in utero* (or postnatally) increases risk of poor performance on neurobehavioral and cognitive examinations during infancy and later in childhood, among those with genetically decreased paraoxonase activity
- Asthma incidence and severity is associated with early life experience with infections
- Nurturing and other behavioral exposures ameliorate or prevent behavioral & developmental disorders associated with genetic polymorphism for serotonin neurotransmitter.



How will Study size produce results not otherwise available?

- Exposures for “big issue” low frequency outcomes
 - Autism
 - Diabetes
 - Still birth
 - Birth defects, etc.
- Sub-groups and multi-factor interactions
 - Obesity
 - Asthma
 - Behavior, etc



Priority Environmental Exposures

- **Physical** environment: housing, neighborhoods and communities, climate, radiation...
- **Chemical** exposures: air, water, soil, food, dust, industrial products, pharmaceuticals...
 - complex ubiquitous low-level exposures
 - unique exposures (special sub-studies)
- **Biological** environment: intrauterine, infection, nutrition; inflammatory and metabolic response...
- **Genetics**: genotype, SNP's, effects of environmental exposures on gene expression...
- **Psychosocial** milieu: influence of family, socio-economics, community, stress...



Priority Outcomes



- **Pregnancy outcome:** preterm birth, birth defects, fetal influences on adult health. **EARLY results!**
- **Neurodevelopment and Behavior:** cognitive development (IQ), autism, learning disabilities, schizophrenia, depression, adjustment, normal variation, resilience...
- **Injury:** intentional and unintentional; violence...
- **Asthma:** envir/genetic/infectious/immune factors..
- **Obesity and Physical Development:** diabetes, pubertal/reproductive development, growth, obesity 'epidemic'...



Sampling and Center strategies



- National probability sample important
 - Exposure-outcome relationship representative of the U.S. population
 - Important exposures with varied and unknown distributions are not missed
- Centers of excellence important
 - Broad scientific input
 - Measures require center expertise and facilities
- Probability sample by Centers
 - Unique combination
 - Requires flexibility and adaptation of center to the scientific design
 - Requires support and guidance by coordinating center



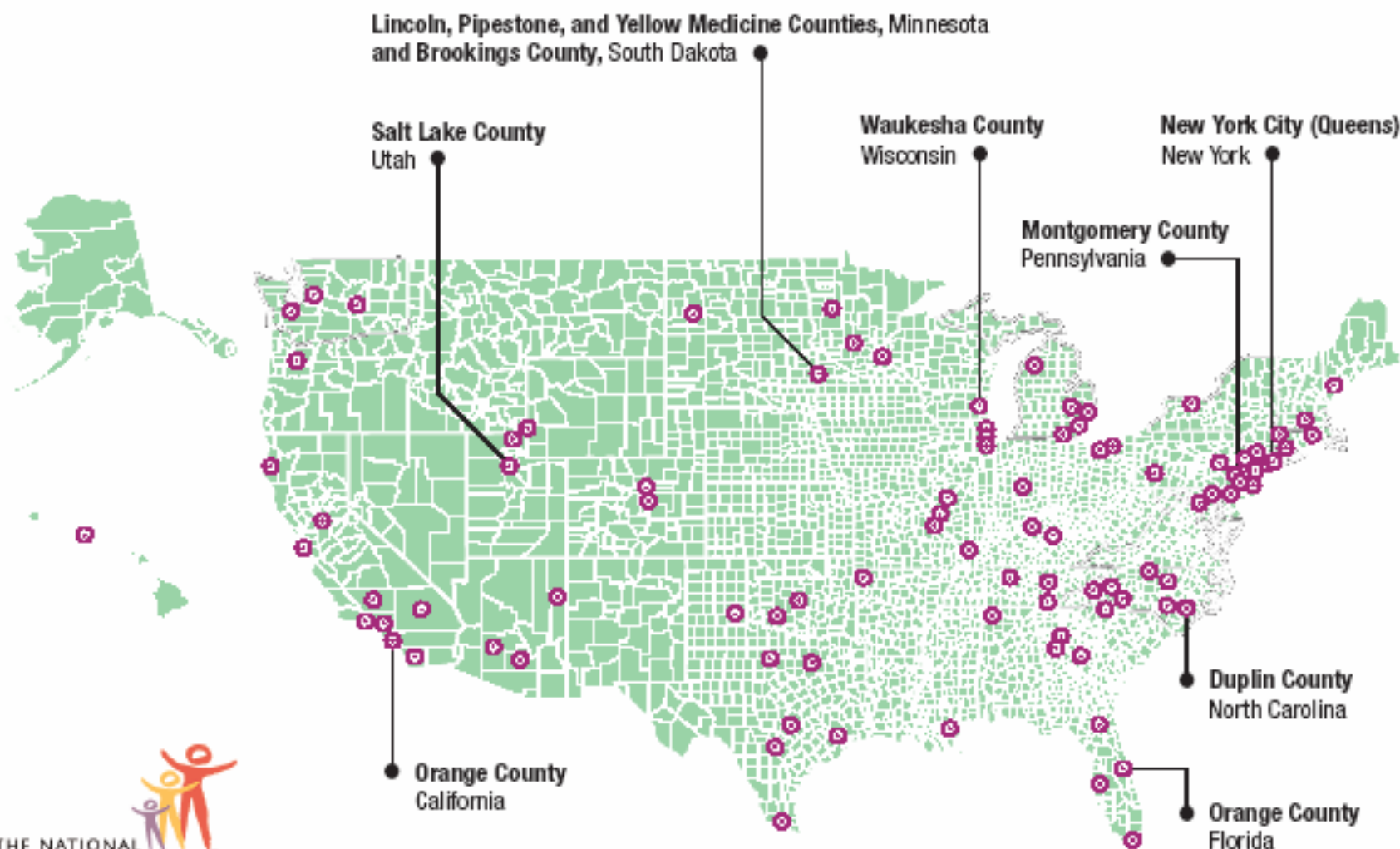
The Sample

- National probability sample
- 96 study locations were drawn from the full list of all counties in the United States
- 13 self representing counties
- Remaining counties were placed into strata based on:
 - Metropolitan status
 - Geography
 - Average number of births per year
 - Race, ethnicity, percent low birth weight



National Children's Study Locations

Vanguard locations identified by name



Selection of Vanguard Locations

- From this list of 96 locations, eight locations were selected to potentially serve as the Vanguard Locations
- 96 locations were placed into strata
 - Geography
 - Metropolitan Status
 - Average number of births per year
 - 2 certainty, 4 metropolitan, non-certainty, 2 non-metropolitan
 - 2 Locations in each of the 4 U.S. Census Regions



National Probability Sample

- Three stages of sample selection
 - Selection of primary sampling units
 - Selection of segments within counties
 - Selection of households/individuals



Selection of Segments

- Several options for defining boundaries of segments
 - Census boundaries
 - Neighborhood boundaries
 - School catchment areas
- Solicit input from the successful offerors to help define the segments
- To maintain the integrity of the sample, offerors will not be involved in the actual selection of segments



Recruitment of Study Participants

- Household Recruitment Approach
- Supplemented with recruitment through other mechanisms such as prenatal care providers
 - Anticipate that some groups of women (e.g. women not planning pregnancy) might be under-represented in the household screening approach
- Offerors can suggest alternative approaches that would meet the goals of The Study



Proposed Schedule of Visits

Screening	18 months (Home)
Preconception	3 years (Clinic)
1 st Trimester (home)	5 years (Clinic)
2 nd Trimester (clinic)	7 years (Home)
3 rd Trimester (clinic)	9 years (Clinic)
Delivery	12 years (Clinic)
1 month (Home)	16 years (Home)
6 months (Home)	20 years (Clinic)
12 months (Home)	



Participating entities



- In place
 - Scientific support reviews, analyses, surveys
 - Information technology development
The prime IT contractor has excluded self from CC
- Over next year
 - Clinical/data coordinating center
 - Initial study centers
- Following
 - Sample Repository
 - Laboratory services



Use of Data to Maximize Output

- Results available beginning ~2010
- Targeted hypotheses-testing analyses
- Successive public-use data sets with support
- Successive funding for investigator initiated research and analyses
- Expected translation of results into related prevention initiatives



Projected Time Line

2000- **Pilot study/methods development work**

Periodically: Meetings, peer reviews, consultations

Mid 2004 Finalize specific hypotheses, develop study design

Late 2005 **Select initial centers**

2006 Complete and pilot full protocol

Early 2007 Enroll first participants with initial centers

2006-2007 **Select additional centers**

2009-2010 First preliminary results available from pregnancy

2007-2030 Analyze data as collection continues, publish results throughout: hypothesis specific, public use datasets, RFA's



Contact Information

- Check the Web site:
<http://NationalChildrensStudy.gov>
- Join the listserv for news and communication
- Contact us at ncs@mail.nih.gov

